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Indium(III)-Catalyzed Tandem Synthesis of 2-Alkynyl-3,3-dichloropyrrolidines and their Conversion to 3-Chloropyrroles

K. Kushwaha,[a] C. C. Malakar,[a] S. Stas,[a] F. Lemière[b] and K. Abbaspour Tehrani[a]*

Abstract

The synthetic utility of electron-deficient α,α,γ-trichloroaldimines was demonstrated by an indium(III) triflate-catalyzed cascade reaction with terminal alkynes allowing one to rapidly and selectively access 2-alkynyl-3,3-dichloropyrrolidines in good to excellent yields. The reaction proceeds in a single synthetic operation *via* an addition of acetylenes to α,α,γ-trichloroaldimines, followed by a spontaneous cyclization of the *in situ* formed trichloropropargylic amines. The dichloromethylene moiety of the aldimine acts as an activating group to accomplish this transformation under very mild conditions. A broad variety of both aryl and alkyl acetylenes, as well as primary and secondary nitrogen substituents in the imine are well tolerated. The dichloromethylene group, which is conserved in the 2-alkynylpyrrolidine enhances the synthetic value of these pyrrolidines and allowed their conversion to (*E/Z*)-2-alkenyl-3-chloropyrroles by a base induced monodechlorination.

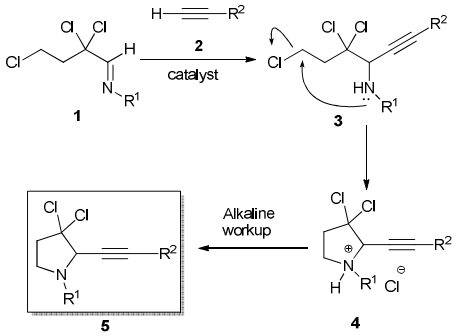
Introduction

The pyrrolidine scaffold is an important core structure due to its widespread use in pharmaceuticals[1] and ubiquity in various natural products[2] as well as biologically active compounds.[3-6] Apart from their importance in medicinal chemistry, pyrrolidines also serve as valuable synthetic intermediates and as reagents.[7] As an example, pyrrolidine based organocatalysts[8] and chiral ligands[9] have been employed in a range of organic transformations.

Herein, we disclose a new, efficient and easy to perform $In(OTf)_3$-catalyzed reaction between α,α,γ-trichloroaldimines and terminal alkynes for the synthesis of a series of highly functionalized 2-alkynylpyrrolidines in good to excellent yields. The reactivity of this new compound subclass was further exploited for the synthesis of 3-chloropyrroles.

In the past years, several elaborate multistep methodologies[10] have been developed for the synthesis of 2-alkynylated pyrrolidines. A direct approach involves the decarboxylative coupling[11] of α-amino acids, such as proline derivatives with alkynes in the presence of Cu(I) as catalyst and a stoichiometric co-oxidant. 2-Alkynyl-2-methylpyrrolidines were prepared by a tandem hydroamination/alkynylation sequence of pent-4-yn-1-amine with terminal alkynes catalyzed by a Au(I) or Cu(I)-catalyst.[12] Other 2-alkyl-2-alkynylpyrrolidines have been made starting from 2-pyrrolidinones[13a] or their corresponding thiolactams[13b] *via* reductive alkylation of the amide functionality with Grignard and organolithium reagents after (thio)lactam activation. In another, elegant approach, the addition of an alkynyl trifluoroborate to the α-position of a pyrrolidine is promoted by the sacrificial reduction of a neighboring carboxaldehyde group.[14]

Finally, a hitherto limited method, makes use of a Shvo-catalyzed alkynylation of amines and pyrrolidine leading to 2-((trimethylsilyl)ethynyl)pyrrolidine.[15]
No reports regarding the synthesis and reactivity of 2-alkynyl-3,3-dihalopyrrolidines are available in the literature. In the present work α,α,γ-trichloroimines were evaluated for the synthesis of 2-alkynylpyrrolidines.
So far, only a few examples involving the synthesis of pyrrolidines using the nucleophile induced cyclization of γ-haloimines have been published.[16] The asymmetric synthesis of 2-arylpyrrolidines has been reported starting from *γ*-chloro-*N*-(tert-butanesulfinyl)ketimines by subsequent reduction of the imine moiety using $NaBH_4$ and then cyclization of the resulting *δ*-chloroamine in the presence of KOH.[17] It is noteworthy that these methods for the synthesis of azaheterocycles rely on the use of strong nucleophiles like cyanide, hydride, hydroxide, alkoxides and only rarely, hard organometallic reagents. Most of these reagents are highly moisture sensitive and have to be used in stoichiometric amounts and therefore the applicability of these methods to highly functionalized substrates is restricted.
Despite the synthetic value of the abovementioned procedures for obtaining 2-alkynylpyrrolidines they rely on either the use of organometallic reagents as the source of the alkyne moiety, on lengthy multistep functional group transformations or suffer from very limited substrate compatibility and availability. Moreover, the introduction of soft carbon nucleophiles in α,α,γ-trichloroimines has never been achieved. Therefore the development of an efficient and mild protocol for the synthesis of 2-alkynylpyrrolidines based on a catalytic reaction of alkynes and suitably substituted imines is a challenging mission.
Consequently, we screened several reaction conditions for the direct addition of terminal alkynes **2** to 2,2,4-trichlorobutanaldimines **1** in the presence of a suitable catalyst (Scheme 1). Intramolecular nucleophile induced cyclization of the obtained polychlorinated propargylic amines **3** (*via* **4**) should further lead to the envisioned 2-alkynyl-3,3-dichloropyrrolidines **5**. The availability of such a convenient preparation of 3,3-dichloropyrrolidines **5**, will allow the further investigation of the reactivity of these highly functionalized compounds (Scheme 1).



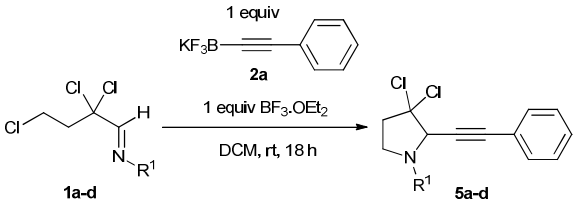
Scheme 1. Proposed synthesis of 2-alkynyl-3,3-dichloropyrrolidines

Results and Discussion

Previously, our research group has reported a convenient synthetic route towards propargylamines by the reaction of *α,α*-dichloroaldimines and potassium alkynyltrifluoroborates

using a Lewis acid-mediated Mannich type reaction.[18] On this basis a reaction was performed between *N*-(2,2,4-trichlorobutylidene)propan-1-amine (**1b**) and potassium phenylethynyltrifluoroborate (**2a**) in the presence of $BF_3.OEt_2$ as Lewis acid (Table 1). After basic workup, the ^1H NMR showed the presence of the desired 3,3-dichloro-1-propyl-2-(phenylethynyl)pyrrolidine (**5b**), besides 10-15% starting material. The use of more equivalents of phenylethynyltrifluoroborate (**2a**), more $BF_3.OEt_2$ or higher reaction temperatures did not lead to better conversions.

Table 1. Synthesis of 3,3-Dichloropyrrolidines Using Alkynyltrifluoroborates[a]



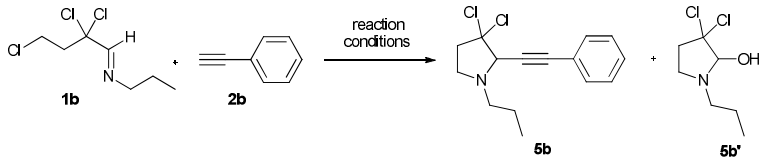
Entry	**1** (R^1)	Product	Yield [%][b]
1	**a** (Et)	**5a**	43
2	**b** (Pr)	**5b**	46
3	**c** (*i*Pr)	**5c**	32
4	**d** (Allyl)	**5d**	40

[a]Reaction was carried out on 0.5 mmol scale. [b]Yield after column chromatography on silica gel.

The pure pyrrolidine (**5b**) was obtained in 46% yield after performing a column chromatography. By utilizing this methodology compounds **5a-d** were synthesized in comparable yields. Besides the rather low yields, there were some disadvantages associated with this protocol. Firstly, the mechanistic studies suggest that the spontaneous cyclization of the initially formed trichloropropargylic amine could not occur during the alkynylation reaction itself due to the formation of non-nucleophilic aminodifluoroborane intermediate (*vide infra*). Therefore the intramolecular nucleophilic substitution will take place only during the workup. Secondly, the fact that the potassium alkynyltrifluoroborate (**2a**) must be prepared in a separate step by metalation of the corresponding alkyne with a highly reactive organometallic reagent (BuLi or LDA) remains a disadvantage. Furthermore, subsequent borylation with $B(OiPr)_3$ is an additional drawback. Therefore we decided to turn to a more efficient and atom economic transition metal-catalyzed addition of a terminal alkyne to these α,α,γ-trichloroaldimines, which would also allow better ring closure of the intermediate trichloropropargylamines **3** towards the desired 3,3-dichloropyrrolidines **5**. During recent years, substantial progress has been made in A^3-coupling reactions. Several transition-metal catalysts have been exploited that activate the C-H bond of the

terminal alkyne. Various metal salts including Cu(I), B(III), Ag(I), Zn(II), Zr(IV), Fe(III), Ni(II), Au(I), Au(III), In(III) and Ir-complexes have been employed as catalysts in the reaction between imines or *in situ* generated imines and the corresponding terminal alkynes or organometallic reagents.[19] Several tandem reactions based on a A^3 coupling as the key transformation have been devised,[20] in particular for the synthesis of more complex and structurally diverse heterocyclic products in one pot.[21] Despite this vivid intrest in A^3 coupling, most methods have a limited scope and are dealing with benzaldehydes or imines derived form benzaldehyde, and never with functionalized aliphatic aldehydes. Moreover, the scarce examples dealing with aliphatic aldehydes/imines even do not carry any functionality to allow further conversions of the formed propargylic amine. Based on our recent contribution,[22] we assume that a Lewis acid activator such as $In(OTf)_3$ needs to activate the imine because of the poor electrophillicity of azomethine carbon as well as to generate the active acetylide as nucleophillic species to accomplish the desired transformation. As a preliminary experiment, 2,2,4-trichlorobutanal and 1 equivalent of propylamine were reacted under typical A^3 coupling conditions in the presence of 25 mol% of $In(OTf)_3$ in DCM as solvent at 50 °C for 18 h. Unfortunately, only 29% conversion to pyrrolidine **5b** was observed besides the corresponding imine **1b** and many unidentified products. Therefore we decided to use the preformed imine, *N*-propyl-(2,2,4-trichloro-1-butylidene)amine (**1b**) for the alkynylation with phenylacetylene (**2b**) with 25 mol% $In(OTf)_3$ as catalyst and dichloromethane as solvent. After basic workup, we were pleased to obtain 67% of 3,3-dichloro-2-(phenylethynyl)-1-propylpyrrolidine (**5b**) (yield calculated by ^{1}H NMR, Table 2, entry 1). In this case, the ^{1}H NMR of the crude reaction mixture also showed 3,3-dichloro-2-hydroxypyrrolidine (**5b'**).

Table 2. Optimization of the Direct Addition of Alkyne (2b) on Aldimine (1b) for the Synthesis of Pyrrolidine (5b)[a]



Entry	Catalyst/[mol%]	Solvent	*t* [°C]	Yield **5b** [%]	Yield **5b'** [%]
1	$In(OTf)_3$/25	DCM	rt	67[b]	20[b]
2	$In(OTf)_3$/25	DCM	rt	68[b,c]	21[b]
3	**$In(OTf)_3$/25**	**DCM**	**50**	**78**[b]	7[b]
4	$InCl_3$/25	DCM	50	21[b]	2
5	InI/25	DCM	50	0	0
6	$Cu(OTf)_2$/25	DCM	50	14[b]	2

7	$Cu(OTf)_2$/25	DCM	50	16[b,c]	1
8	$Cu(OTf)_2$/25	PhMe	80	13[b,c]	3
9	CuBr/25	DCM	50	5[b]	0
10	$Cu(OAc)_2$/25	DCM	50	7[b]	0
11	AgOTf	DCM	50	23[b]	4
12	$Sc(OTf)_3$/25	DCM	50	23[b]	2
13	$FeCl_3$/25	DCM	50	0	0

[a]Unless otherwise mentioned, all reactions were performed using 0.5 mmol **1b** with 0.5 mmol **2b** in DCM (4 mL) in a sealed vial under air for 18h. [b] Calculated from ^{1}H NMR after basic workup. [c]Reaction performed under argon.

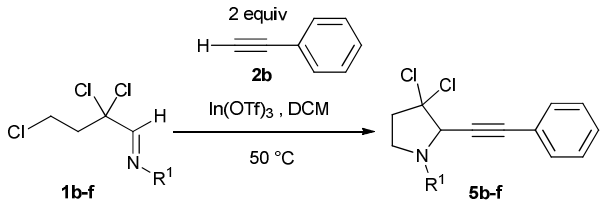
(20% yield). This hemiaminal (**5b'**) is probably formed from unreacted imine during the aqueous basic work up.[23] To avoid the formation of this unreactive hemiaminal **5b'** and to increase the yield, the same reaction was repeated under argon, but that did not lead to any improvement. However, heating the reaction mixture at 50 °C significantly increased the yield to 78% and the formation of **5b'** could be suppressed (Table 2, entry 3). To observe the influence of other indium salts, we used $InCl_3$ and InI. Only $InCl_3$ was found successful in accomplishing the desired transformation in 21% yield, whereas the reaction mixture obtained in the presence of InI was complex and did not show any formation of the product (Table 2, entries 4 and 5). Further screening of the reaction conditions in DCM was executed using frequently used copper salts such as $Cu(OTf)_2$, CuBr and $Cu(OAc)_2$. Among these, $Cu(OTf)_2$ could result in the formation of the desired product **5b** but in only 16% yield whereas CuBr and $Cu(OAc)_2$ result in even lower yields (Table 2, entries 6-10). The low yields with copper salts can be attributed to side reactions such as homocoupling of phenylacetylene, which proceed under air and poor activation of the imine **1b** by the copper salt. Replacing the air by argon and by using $Cu(OTf)_2$ in dichloromethane or toluene at higher temperature did not improve the reaction (Table 2, entries 7 and 8). Although AgOTf and $Sc(OTf)_3$ as Lewis acids were also able to carry out this transformation, yields were still low as compared to $In(OTf)_3$ (Table 2, entries 11 and 12). $FeCl_3$ failed completely to perform this reaction. In all the cases discussed above, the formation of an open chain product **3** was never observed.

The reason that In(III) salts behave superior in this alkynylation reaction may be found in the hardness of indium(III). Since In(III) is a hard acid and the imine nitrogen is a soft base[24], the Lewis acid activation of the imino nitrogen by indium is not plausible. During the formation of the acetylide from the the terminal alkyne and $In(OTf)_3$ triflic acid is formed, which will enhance the electrophilic character of the imine by protonation of the nitrogen, and hence facilitating the acetylide addition across the C=N bond. Further it has been determined that $InBr_3$ (supposingly $InCl_3$ behaves the same) forms indium(III) acetylide, while indium(III) triflate was proven to form indium(III) diacetylides, which are more effective in transferring the acetylene moiety.[25] Copper(I) will also form acetylides but as Cu(I) is a soft acid it will complex to the soft imino

nitrogen, thus preventing the acetylide to add efficiently to the C=N bond, because of a wrong orientation of the acetylide moiety.

Having established the importance of $In(OTf)_3$ in this transformation and in order to find optimal conditions more experiments were carried out using $In(OTf)_3$ as catalyst but with modified reagent ratios and different solvents (See SI for further optimization).
Based on the results of the catalyst screening (Table 2) and optimization experiments with $In(OTf)_3$ (see SI), the best reaction conditions were to perform the conversion in the presence of 25 mol% of $In(OTf)_3$ as catalyst in DCM with an excess of the alkyne at 50 °C in a sealed vial for 18-24h. Under these conditions most of the pyrrolidines **5** could be obtained as pure compounds without extra purification step required. Next, the scope of this $In(OTf)_3$ mediated transformation with respect to the nitrogen substituent of the imines was studied. We were gratified to discover that along with the propyl group, the reaction worked well with other substituents such as allyl, *n*-butyl and isopropyl (Table 3). For *n*-butyl and allyl groups a yield of 82% and 84% was achieved respectively (Table 3, entries 3 and 4). With the N-isopropyl imine a slightly higher temperature (55-60 °C) and longer reaction time (24h) was required in order to achieve complete conversion to the corresponding pyrrolidine **5c** (entry 2). In all these cases, no open chain products were observed. With the even more sterically demanding N-*tert*-butyl imine **1f**, the reaction mixture only showed the presence of the ring closed product in trace amounts, besides some undefined signals, and mainly the formation of corresponding hemiaminal **5f'** was observed.

Table 3. $In(OTf)_3$-Mediated Synthesis of 5 Using Various α,α,γ-Trichloroaldimines[a]

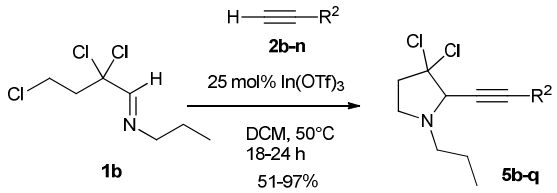


Entry	**1** (R^1)	Product **5**	Yield [%][b]
1	**b** (Pr)	**b**	80[b]
2	**c** (*i*Pr)	**c**	65[c]
3	**d** (Allyl)	**d**	82[b]
4	**e** (*n*-Bu)	**e**	84[b]
5	**f** (*t*-Bu)	**f**	trace

[a]All reactions were performed using 0.5 mmol **1** with 2 equiv **2b** in DCM (4 mL) in a sealed vial under air for 18-24 h. [b]Isolated yields after basic workup. [c] Yield after chromatography using a short column of silica gel.

We further extended the scope of this reaction to include aryl acetylenes (Table 4). A variety of electron-donating substituents such as *ortho*- and *para*- methyl and ethyl groups were well tolerated under the optimized reaction conditions and the corresponding products **5f-h** were obtained in good yields from 68-72% (Table 4, entries 2-4). Electron withdrawing substituents such as chloro, bromo, 3-methoxy and fluoro groups (in the presence of a methyl) were also well survived and afforded the corresponding products **5i-l** in slightly lower yields in comparison to electron donating groups (Table 4, entries 5-8). The reaction of **1b** with 2-nitrophenylacetylene did not result in the desired compound and ^{1}H NMR indicated mainly the presence of unreacted 2-nitrophenylacetylene and hemiaminal **5b'**.

Table 4. In(OTf)$_3$-Mediated Synthesis of 5b-h Using Various Terminal Acetylenes[a]



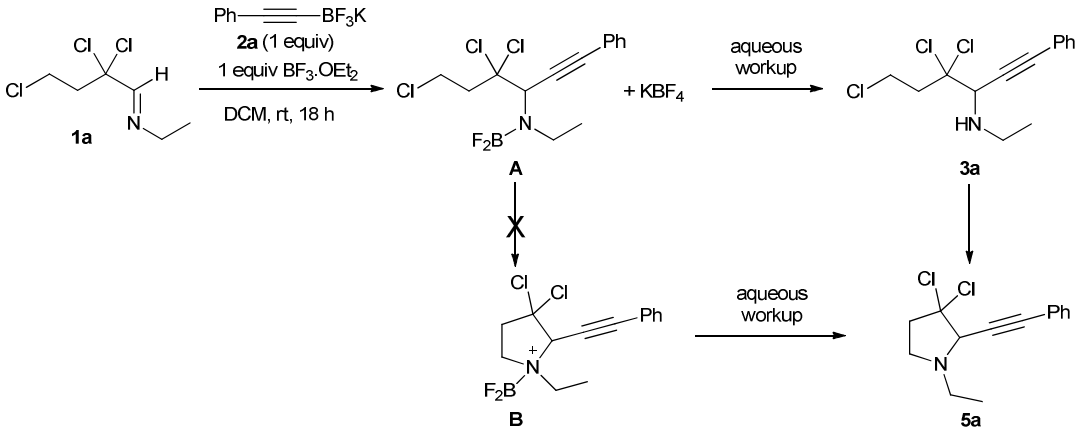
Entry	Alkyne **2** (R^2)	Product **5**	Yield [%]
1	**2b** (C_6H_5)	**5b**	80[b]
2	**2c** (2-Me-C_6H_4)	**5f**	68[c]
3	**2d** (4-Me-C_6H_4)	**5g**	71[c]
4	**2e** (4-Et-C_6H_4)	**5h**	72[c]
5	**2f** (3-MeO-C_6H_4)	**5i**	71[b]
6	**2g** (4-Cl-C_6H_4)	**5j**	62[c]
7	**2h** (4-F-3-Me-C_6H_3)	**5k**	54[c]
8	**2i** (4-Br-C_6H_4)	**5l**	51[c]
9	**2j** (cHex)	**5m**	97[b,d]
10	**2k** (cPent)	**5n**	77[b,d]
11	**2l** (Pr)	**5o**	77[b,d]

12	**2m** (*n*-Bu)	**5p**	74[b,d]
13	**2n** (*t*-Bu)	**5q**	70[b,d]

[a]All reactions were performed using 0.5 mmol **1b** and 2 equiv **2** in DCM (4 mL) in a sealed vial under air for 18 h. [b] Isolated yield after basic workup. [c] Yield after chromatography using a short column of silica gel. [d] Reaction for 24 h.

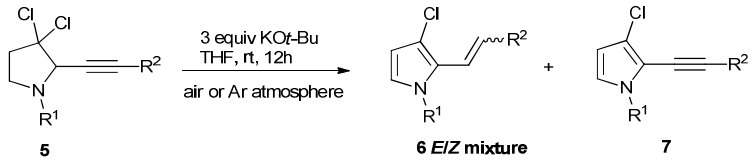
Apart from arylacetylenes, also a number of acyclic and cyclic aliphatic acetylenes **2j-n** was evaluated (Table 4). With cyclohexylacetylene (**2j**) an excellent 97% yield was obtained for compound **5m** (entry 9). With cyclopentylacetylene (**2k**) and other aliphatic acetylenes good yields (70-77%) of nearly pure pyrrolidines were also obtained after simple aqueous basic workup (Table 4, entries 10-13). The open chain intermediate **3** was not isolated or even observed in the ^{1}H NMR spectra of the crude reaction mixture after workup in any of the abovementioned pyrrolidine syntheses. In this context the ^{1}H NMR of the reaction mixture after non-aqueous workup was recorded. A very broad peak around 5 ppm accounts for the NC*H*CCl_2 proton and this downfield shift, compared to the NC*H*CCl_2 proton (4.11 ppm) of **5b** is indicative for a positively charged nitrogen atom. A comparison was made of this spectrum with the ^{1}H NMR of an independently prepared sample of the hydrochloride of pyrrolidine **5b**. Since both spectra were not the same, it can be concluded that most probably pyrrolidine **5b** formed a complex with $In(OTf)_3$ during the reaction.

The mechanism for the formation of 3,3-dichloropyrrolidines **5** using alkynyltrifluoroborates is different (Scheme 2). It has been established that the reaction of chlorinated aldimines with potassiumtrifluoroborates results in an aminodifluoroborane intermediate which upon aqueous workup gives the chloroamine.[18] Since the aminodifluoroborane nitrogen atom in intermediate **A** is less nucleophilic it is expected that ring closure cannot take place after the addition of the alkyne moiety to the imino carbon. As a consequence the ring closure must occur during the aqueous workup. In order to prove the existence of an intermediate aminodifluoroborane **A**, the reaction mixture obtained after Petasis reaction of *N*-(2,2,4-trichloro-1-butylidene)ethylamine (**1a**), potassium phenylethynyl-trifluoroborate (**2a**) and $BF_3{\cdot}OEt_2$, was filtered, evaporated and analysed by ^{1}H, ^{19}F and ^{11}B NMR. The solid, which was filtered off prior to evaporation was shown to be KBF_4 by comparison with a commercially available reference sample. The signals in the ^{1}H NMR ($CDCl_3$) of the filtrate after evaporation were shifted downfield compared to the signals of 3,3-dichloro-2-phenylethynylpyrrolidine (**5a**), pointing to the existence of an aminodifluoroborane intermediate **A**. Especially, the signal at 3.78 ppm is characteristic for a Cl*C*H_2 and not a N*C*H_2, indicating the presence of non-ring closed Mannich product. These results confirm the earlier stated assumption that first aminodifluoroborane **A** is formed and that ring closure takes only place during aqueous workup. A second experiment was executed to confirm the obtained results. The NMR sample of the filtrate was treated with a few drops of water and the ^{1}H NMR was recorded again to check if trichlorinated Mannich product **3a** was present. In this case the formation of pyrrolidine **5a** (18%) and **3a** (82%) was observed. The presence of the latter was interpreted by an upfield shift of all the NMR-signals compared to the signals of aminodifluoroborane **A** (striking shift for CCl_2C*H*N from 5.00 ppm (**A**) to 4.80 ppm (**3a**)). The ease of cyclization of trichloroamines **3** is probably due to the Thorpe-Ingold effect and is therefore not affected by the presence of indium(III).



Scheme 2. Mechanism for the formation of 3,3-dichloropyrrolidines using alkynyltrifluoroborates

Table 5. Synthesis of 2-Alkenyl-3-chloropyrroles 6 from Pyrrolidines 5[a]

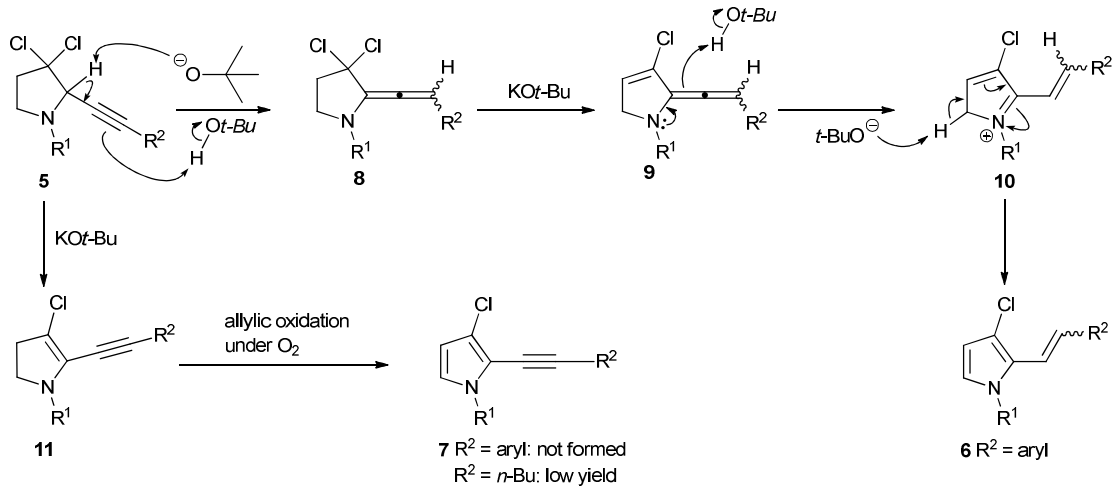


Entry	**5** (R^1)	Product **6** (*E*/*Z*)	Yield [%]
1	**b** (Pr)	**6a/6b** (1:1.2)	90
2	**e** (*n*-Bu)	**6c** (1:1.4)	95
3	**g** (Pr)	**6d** (1:1.1)	65
4	**i** (Pr)	**6e** (1:1.4)	88
5	**k** (Pr)	**6f** (1:1.1)	86
6[b]	**p** (Pr)	**7**	7

[a]All reactions were performed on 0.25 mmol of pyrrolidines **5** and 0.75 mmol of KO*t*-Bu in THF (5 mL).
[b]Reaction was performed on 0.34 mmol scale.

Along with pyrrolidines, halogenated pyrroles are known to be important constituents of many bioactive compounds isolated from natural sources[26] and possess diverse physiological activities[27] and thus have acquired a prominent place in pharmaceutical sciences. Besides their interesting biological activities, more specifically 3-halopyrroles have been used in cross-coupling reactions.[28] Several 3-halopyrroles have been made by base-induced aromatization reactions of 3,3-dihalo-1-pyrrolines, which were prepared by multistep protocols.[29] So far, 3,3-dihalopyrrolidines never have been converted to the corresponding 3-halopyrroles.

Therefore, after developing a successful methodology for the synthesis of 3,3-dichloropyrrolidines our interests focussed on converting these pyrrolidines into 3-halopyrroles (Table 5). Pyrrolidine **5b** was reacted with 3 equivalents of NaOMe in methanol, but side products were detected in the ^{1}H NMR spectrum. By reacting **5b** with 3 equivalents of the more sterically hindered KO*t*-Bu in THF (Method A), a pyrrole nucleus containing compound **6a/b** was isolated in an excellent 84% yield (Table 5, entry 1).
Analysis of the ^{1}H NMR spectrum however proved that the expected 2-alkynyl-3-chloropyrrole **7** was not formed but suggested the formation of an *E*/*Z* mixture of 2-alkenylpyrroles **6a/b** in a 1:1.2 ratio. Separation of this mixture by means of column chromatography resulted in few pure fractions of *E*-**6a** and mostly a pure mixture of *E/Z*-**6a/b** was isolated. The fact that the rotational barrier around a heteroaromatic substituted alkene is lowered by resonance, lead to isomerisation of the alkene during the ^{13}C NMR measurement. Therefore the *E* and *Z* isomers were not separated for other 2-alkenylpyrroles. This aromatization reaction could be extended to prepare a variety of 2-(2-arylvinyl)pyrroles in excellent yields. In none of these cases were 2-alkynylpyrroles **7** observed in the crude reaction mixture. As an exception, the reaction of 3,3-dichloro-2-(hex-1-ynyl)pyrrolidine (**5p**) with KO*t*-Bu in THF can be mentioned. A very complex reaction mixture was obtained, which only after tedious chromatography furnished a small amount (7%) of 3-chloro-2-(hex-1-ynyl)-1-propyl-1*H*-pyrrole **7**. Other pyrrolidines (**5m**, **5n**), derived from aliphatic alkynes, also gave rise to complex mixtures under these conditions and were therefore not further investigated.
The formation of the 2-alkenylpyrrole **6** may be explained by an initial deprotonation of the propargylic C-H of **5** with KO*t*-Bu, leading to a propargyl-allenyl anion, which is immediately reprotonated by *t*-butanol to afford the allene **8**. This compound undergoes a base promoted 1,2-dehydrochlorination, followed by an allenamine-iminium tautomerism furnishing the alkenyl-substituted 2*H*-pyrrolium **10**. Finally a base promoted bond isomerisation yields the 2-alkenylpyrrole **6**. A similar alkyne-alkene isomerisation via an allenic intermediate has been reported in other cases.[30] The alternative route may pass via a base promoted dehydrochlorination of the 3,3-dichloropyrrolidine. The obtained 3-chloro-2-pyrroline **11**[29a-b] may undergo an allylic autooxidation (Scheme 2) followed by elimination of water to give 2-alkynylpyrrole **7**. In case of R^2 = aryl, the allene route is more favoured because of resonance stabilization (Scheme 3).

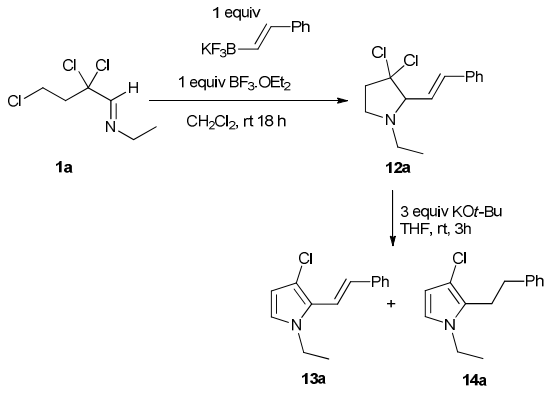


Scheme 3. Plausible mechanism for the base promoted aromatization of 2-alkynyl-3,3-dichloropyrrolidines

In order to evaluate if the base induced shift of the external double bond is also occurring in other systems, the analogous 3,3-dichloro-2-styrylpyrrolidine **12a** was synthesized. For that purpose *N*-(2,2,4-trichloro-1-butylidene)amine **1a** was reacted overnight with one equivalent of potassium (2-phenyl)vinyltrifluoroborate and $BF_3.OEt_2$ at room temperature in dichloromethane with HFIP as cosolvent (9/1) (Table 6, entry 1). After alkaline aqueous workup, the corresponding (*E*)-3,3-dichloro-2-(2-phenylvinyl)pyrrolidine **12a** could be identified besides 10% starting imine **1** and 12% 3,3-dichloro-2-hydroxypyrrolidine. Flash chromatography of the crude mixture on silica gel resulted in the pure, solid pyrrolidine **12a**. No further optimization reactions were performed since the envisioned compound was obtained in sufficient quantities for studying the aromatization reaction.

The small scale reaction of 3,3-dichloro-2-styrylpyrrolidine **12a** with potassium *tert*-butoxide in THF furnished the corresponding 3-chloro-2-styrylpyrrole **13a** as the major compound and of 3-chloro-2-(2-phenylethyl)pyrrole **14a** as the minor component. Interestingly, when the reaction of 3,3-dichloro-2-styrylpyrrolidine 1**2a** with KO*t*Bu was scaled up from 0.5 mmol to 1.85 mmol, the amount of the side product **14a** increased drastically (Table 6, entry 2). A possible explanation for this observation might be found in the occurrence of oxygen-limitation in the bigger reaction volume, leading to less allylic autooxidation of the intermediate 3-chloro-2-pyrroline **8** and hence less formation of 3-chloro-2-styrylpyrrole **10a**. Consequently, the double bond of the olefinic substituent will migrate into the ring and will give rises to the stable aromatic pyrrole. To further support this statement, the same large scale experiment was repeated under exactly the same conditions except that dry compressed air was bubbled through the reaction mixture. The amount of **14a** now drastically decreased in favor of 2-styrylpyrrole **13a** (Table 6, entry 3). These observations are in accordance with the reaction mechanism depicted in Scheme 2. The fact that the reaction of 2-alkynyl-3,3-dichloropyrrolidines with KO*t*Bu is less oxygen dependent compared to 3,3-dichloro-2-styrylpyrrolidines can be explained by the fact that the former under all conditions (aerobic or anaerobic) will lead to resonance stabilized pyrroles.

Table 6. Synthesis of 3,3-Dichloro-1-ethyl-2-styrylpyrrolidine and the Corresponding 3-Chloropyrroles



Entry	Yield **12a** [%][a,b]	Yield **13a** [%][b]	Yield **14a** [%][b]
1	57	45[c]	2[c]
2	-	20[d]	35[d]
3	-	25[e]	2[e]

[a]Reactions were performed on 0.5 mmol scale. [b]Yield after chromatography on silica gel. [c]Reaction was performed on 0.5 mmol of pyrrolidine **12a** and 0.75 mmol of KO*t*-Bu in THF (4 mL). [d]Reaction was performed on 1.85 mmol of pyrrolidine **12a** and 5.55 mmol of KO*t*-Bu in THF (15 mL). [e]Reaction was performed on 1.85 mmol of pyrrolidine **12a** and 5.55 mmol of KO*t*-Bu in THF (15 mL) and by bubbling air through the reaction mixture.

Conclusion

In summary, an efficient and operationally simple method for the synthesis of 2-alkynyl-3,3-dichloropyrrolidines from imines and readily available acetylenes has been developed using indium(III) triflate as a Lewis acid. The reaction proceeds in a single synthetic operation *via* indium(III) catalyzed addition of acetylenes to α,α,γ-trichloroaldimines, followed by a spontaneous cyclization of the *in situ* formed trichloropropargylic amines to form a wide variety of pyrrolidines in good to excellent yields and in high purity. Notably, the traditional reaction conditions for alkynylation of imines were unable to accomplish the alkynylation reaction. The dichloromethylene moiety of the aldimine acts as an activating group to accomplish this transformation under very mild conditions. As the dichloromethylene group, is conserved in the 2-alkynylpyrrolidine, the reactivity of these highly functionalized pyrrolidines with regard to their conversion into 3-chloropyrroles was closely investigated. Remarkably, the reaction of 2-alkynyl-3,3-dichloropyrrolidines with KO*t*-Bu led exclusively to 2-alkenyl-3-chloropyrroles. This is in sharp contrast with the analogous reaction of a 2-alkenyl-3,3-dichloropyrrolidine with KO*t*-

Bu which gives also 2-alkenyl-3-chloropyrrole next to substantial amounts of 2-alkyl-3-chloropyrrole.

Experimental Section

General remarks and instrumentation

All acetylenes were purchased from commercial suppliers (Sigma-Aldrich Chemical Co., Acros Organics, Alfa-Aesar). Phenylethynyltrifluoroborate was synthesized by deprotonation of phenylacetylene (**2a**) with *n*BuLi followed by transmetallation to boron with trimethylborate and *in situ* treatment with KHF_2 according to the literature procedure.[31] All reactions were carried out under air in oven-dried 10 mL microwave vials. Solvents used in extraction and purification were distilled prior to use. Products were purified by column chromatography using silica gel as an adsorbent. ^{1}H (^{13}C) NMR spectra were recorded at 400 (100) MHz using $CDCl_3$ as solvent with TMS as the internal standard. The ^{13}C chemical shifts were referenced to residual solvent signals at δ_C 77.00 ($CDCl_3$). 2D Experiments (COSY, HMQC and HMBC) were carried out for two compounds as examples and data are given for further supporting the structure of the final compounds. *J* values are given in Hertz (Hz) and chemical shifts are given in ppm. For high resolution mass spectrometric analysis, samples were dissolved in CH_3CN and diluted to a concentration of approximately 10^{-5} mol/L.

General experimental procedure for the synthesis of α,α,ω-trichloroaldimines

The α,α,ω-trichloroaldimines **1a-f** were prepared from 2,2,4-trichlorobutanal[32] with different primary amines under $TiCl_4$ activation according to a previously reported method.[33] Since the N-alkyl imines **1** are hydrolytically unstable, no molecular ion peak was observed during HRMS measurement. Instead, the $[M+H^+]$ for the product resulting from nucleophilic addition of water to the C=N bond followed by intramolecular nucleophilic substitution, was observed. Therefore the HRMS for the 1-alkyl-3,3-dichloro-2-hydroxypyrrolidines are reported for **1a-d, f**.

N-(2,2,4-Trichloro-1-butylidene)ethylamine (1a): scale: 11.4 mmol; colorless liquid; yield: (0.74 g, 32%); bp = 24-26 °C/0.009 mmHg. **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.23 (t, 3H, *J* = 7.3 Hz, $NCH_2C\mathbf{H_3}$), 2.96-2.89 (m, 2H, $C\mathbf{H_2}CCl_2$), 3.54 (qd, 2H, J_1 = 7.3 Hz, J_2 = 1.3 Hz, $NC\mathbf{H_2}CH_3$), 3.86-3.80 (m, 2H, $ClC\mathbf{H_2}$), 7.72 (t, 1H, *J* = 1.3 Hz, **H**C=N). **^{13}C NMR** (62.90 MHz, $CDCl_3$): δ = 15.3, 39.3, 46.0, 53.7, 85.7 (**C**Cl_2), 158.3 (**C**=N). **IR** (ATR, cm^{-1}): ν = 1666 (**C=N**). **MS** (70 eV, *m/z* (%)): 208 ($[M+7]^+$, 0.1), 206 ($[M+5]^+$, 0.67), 204 ($[M+3]^+$, 5), 202 ($[M+H^+]$, 5), 166 (14), 141 (15), 139 (26), 126 (11), 124 (20), 116 (14), 111 (12), 109 (16), 102 (37), 87 (17), 85 (17), 83 (12), 80 (17), 78 (12), 77 (12), 75 (49), 73 (24), 68 (25), 67 (21), 64 (15), 63 (10), 61 (32), 56 (100), 54 (16), 53 (15), 51 (60). **HRMS** (ESI) for 3,3-dichloro-1-ethyl-2-hydroxypyrrolidine: *m/z* Calcd for $C_6H_{11}Cl_2NO+H^+$: 184.0290; Found 184.0285.

N-(2,2,4-Trichlorobutylidene)propan-1-amine (1b): scale: 11.4 mmol; colorless liquid; yield: (1.48 g, 60%); bp = 46-50 °C/0.1 mmHg. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.91 (t, 3H, *J* = 7.6 Hz), 1.65 (sextet, 2H, $NCH_2C\mathbf{H_2}CH_3$), 2.91-2.95 (m, 2H, *J* = 7.6 Hz, $C\mathbf{H_2}CCl_2$), 3.46 (td, 2H, J_1 = 6.8 Hz, J_2 = 1.2 Hz, $NC\mathbf{H_2}CH_2CH_3$), 3.80-3.84 (m, 2H, $ClC\mathbf{H_2}$, *J* = 7.6 Hz), 7.71 (t, 1H, *J* = 1.3 Hz, **H**C=N). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.5, 23.3, 39.3, 46.0, 61.0, 85.7 (**C**Cl_2), 158.7

(**C**=N). **IR** (ATR, cm^{-1}): ν = 1670 (**C=N**). **HRMS** (ESI) for 3,3-dichloro-2-hydroxy-1-propylpyrrolidine (**5b'**): *m/z* Calcd for $C_7H_{13}Cl_2NO+H^+$: 198.0447; Found 198.0442.

N-(2,2,4-Trichlorobutylidene)propan-2-amine (1c): scale: 11.4 mmol; colorless liquid; yield: (1.38 g, 56%); bp = 28-32 °C/0.01 mmHg. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.18 (d, 6H, J = 6.4 Hz, $CH(CH_3)_2$), 2.91-2.95 (m, 2H, CH_2CCl_2), 3.49 (septet, 1H, J = 6.3 Hz, $CH(CH_3)_2$), 3.81-3.85 (m, 2H, $ClCH_2$), 7.71 (s, 1H, HC=N). **^{13}C NMR** (62.90 MHz, $CDCl_3$): δ = 23.2, 39.2, 45.8, 59.5, 85.7 (CCl_2), 156.1 (**C**=N). **IR** (ATR, cm^{-1}): ν = 1662 (**C=N**). **MS** (70 eV, *m/z* (%)): 222 ($[M+7]^+$, trace), 220 ($[M+5]^+$, 0.1), 218 ($[M+3]^+$, 0.9), 216 ($[M+H^+]$, 1), 153 (13), 140 (16), 138 (25), 102 (14), 75 (22), 70 (100), 68 (12), 63 (20), 61 (14), 51 (39). **HRMS** (ESI) for 3,3-dichloro-2-hydroxy-1-isopropylpyrrolidine (**5c'**): *m/z* Calcd for $C_7H_{13}Cl_2NO+H^+$: 198.0447; Found 198.0445.

N-(2,2,4-Trichlorobutylidene)prop-2-en-1-amine (1d): scale: 11.4 mmol; colorless liquid; yield: (1.27 g, 52%); bp = 34-38 °C/0.007 mmHg. **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 2.92-2.98 (m, 2H, CH_2CCl_2), 3.81-3.88 (m, 2H, $ClCH_2$), 4.13-4.17 (m, 2H, NCH_2-CH=CH_2), 5.14-5.23 (m, 2H, NCH_2-CH=CH_2), 5.89-6.04 (m, 1H, NCH_2-CH=CH_2), 7.75 (t, 1H, J = 1.5 Hz, HC=N). **^{13}C NMR** (62.90 MHz, $CDCl_3$): δ = 39.3, 46.0, 61.1, 85.7 (CCl_2), 117.2, 134.0, 159.8 (**C**=N). **IR** (ATR, cm^{-1}): ν = 1667 (**C=N**), 1426, 1355 (**CH=CH$_2$**). **MS** (70 eV, *m/z* (%)): 220 ($[M+7]^+$, trace), 218 ($[M+5]^+$, 0.5), 216 ($[M+3]^+$, 1), 214 ($[M+H^+]$, 2), 151 (19), 116 (27), 111 (17), 109 (27), 101 (12), 87 (20), 85 (20), 83 (31), 80 (11), 77 (11), 75 (35), 73 (15), 68 (100), 63 (10), 61 (22), 53 (12), 52 (11), 51 (51). **HRMS** (ESI) for 1-allyl-3,3-dichloro-2-hydroxypyrrolidine: *m/z* Calcd for $C_7H_{11}Cl_2NO+H^+$: 196.0290; Found 196.0328.

N-(2,2,4-Trichlorobutylidene)butan-1-amine (1e): scale: 11.4 mmol; colorless liquid; yield: (1.55 g, 59%). The imine was used as such without any purification, because of its lability. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.93 (t, 3H, J = 7.2 Hz, $NCH_2CH_2CH_2CH_3$), 1.33 (sextet, 2H, J = 7.2 Hz, $NCH_2CH_2CH_2CH_3$), 1.60 (quintet, 2H, J = 7.2 Hz, $NCH_2CH_2CH_2CH_3$), 2.91-2.95 (m, 2H, CH_2CCl_2), 3.41 (td, 2H, J_1 = 6.8 Hz, J_2 = 1.2 Hz, $NCH_2CH_2CH_2CH_3$), 3.80-3.84 (m, 2H, $ClCH_2$), 7.71 (s, 1H, HC=N). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 13.6, 20.1, 32.0, 39.2, 45.9, 59.0, 85.6 (CCl_2), 158.5 (**C**=N). **IR** (ATR, cm^{-1}): ν = 1686 (**C=N**). No molecular ion peak was observed for the corresponding 1-butyl-3,3-dichloro-2-hydroxypyrrolidine.

N-t-Butyl-(2,2,4-trichloro-1-butylidene)amine (1f): scale: 11.4 mmol; colorless liquid; yield: (1.47 g, 56%); bp = 33-37 °C/0.005 mmHg. **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.21 (s, 9H, $C(CH_3)_3$), 2.91-2.97 (m, 2H, CH_2CCl_2), 3.79-3.86 (m, 2H, $ClCH_2$), 7.61 (s, 1H, HC=N). **^{13}C NMR** (62.90 MHz, $CDCl_3$): δ = 28.9, 39.5, 45.8, 57.2, 86.7 (CCl_2), 153.5 (**C**=N). **IR** (ATR, cm^{-1}): ν = 1659 (**C=N**). **MS** (70 eV, *m/z* (%)): 236 ($[M+7]^+$, 0.1), 234 ($[M+5]^+$, 0.2), 232 ($[M+3]^+$, 0.9), 230 ($[M+H^+]$, 1), 216 (22), 214 (22), 167 (15), 140 (16), 138 (28), 134 (11), 130 (15), 113 (15), 111 (26), 87 (13), 84 (56), 79 (18), 77 (39), 75 (17), 73 (13), 63 (14), 61 (14), 57 (100), 53 (13), 51 (40). **HRMS** (ESI) for 1-*t*-butyl-3,3-dichloro-2-hydroxypyrrolidine (**5f'**): *m/z* Calcd for $C_8H_{15}Cl_2NO+H^+$: 212.0603; Found 212.0619.

General experimental procedure (I) for the In(III)-mediated synthesis of 2-alkynyl-3,3-dichloropyrrolidines (5b-q): In an oven dried 10 mL microwave vial, imines (**1b-e**) (0.5 mmol, 1 equiv), acetylenes (**2b-n**) (1.0 mmol, 2 equiv) and $In(OTf)_3$ (0.125 mmol, 70.3 mg, 0.25 equiv) were added successively and the vial was sealed with a pressure cap under air. Subsequently,

DCM (4 mL) was added and the reaction mixture was placed in a preheated oil bath at 50 °C and allowed to reflux for 18-24 h. In case of alkyl acetylenes the reaction mixture was heated for 24 h. Afterwards, the reaction mixture was cooled down, diluted with DCM (5 mL) and extracted with 0.5 N NaOH (5 mL) solution. The remaining aqueous layer was extracted with DCM (2 × 4 mL). Combined organic layers were dried using $MgSO_4$, filtered and solvent was evaporated under reduced pressure to afford pure pyrrolidines **5b-q**. However if required, the crude reaction mixture was subjected to column chromatography using a short path of silica gel (column diameter 1 cm, length 10 cm) to afford the corresponding pyrrolidines as yellow oils.

General experimental procedure (II) for the borontrifluoride mediated synthesis of 2-alkynyl-3,3-dichloropyrrolidines (5a-d): To a stirred solution of the imines (**1a-d**) (0.5 mmol, 1 equiv) in DCM (4 mL), potassium phenylethynyltrifluoroborate (0.5 mmol, 104 mg, 1 equiv) was added in one portion, followed by $BF_3.OEt_2$ (0.5 mmol, 71 mg, 1 equiv). The reaction mixture was stirred for 18 h at room temperature. Afterwards, the reaction mixture was poured into aqueous 0.5 N NaOH. After isolation of the organic layer, the aqueous phase was washed with DCM (4 × 4 mL). The organic fractions were dried using $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to obtain pure 3,3-dichloropyrrolidines **5a-d**.

3,3-Dichloro-1-isopropylpyrrolidin-2-ol (5c'): According to the general procedure I, *N*-(2,2,4-trichlorobutylidene)isopropylamine (**1c**) (0.5 mmol, 115 mg), phenylacetylene (**2b**) (0.5 mmol, 51 mg) and $In(OTf)_3$ (0.125 mmol, 70 mg) were reacted in DCM (4 mL) in a sealed vial at 50 °C for 18 h. Alkaline work up and column chromatography afforded 16% of **5c'** as a white solid. R_f = 0.35 (*n*-hexane/ethyl acetate 90/10). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.11 (d, 3H, J = 6.5 Hz, $CH(CH_3)_2$), 1.14 (d, 3H, J = 6.5 Hz, $CH(CH_3)_2$), 2.14 (CHO**H**), 2.54-2.66 (m, 2H, CH_2CCl_2), 2.88-2.95 (m, 1H, CH_aH_bN), 3.13 (septet, 1H, J = 6.4 Hz, $CH(CH_3)_2$), 3.05-3.11 (m, 1H, CH_aH_bN), 4.70 (s, 1H, $NCHCCl_2$). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 20.0, 21.1, 42.3, 44.4, 50.0, 91.5, 92.0. **HRMS** (ESI): *m/z* Calcd for $C_7H_{13}Cl_2NO+H^+$: 198.0447; Found 198.0451.

1-tert-Butyl-3,3-dichloro-2-hydroxypyrrolidine (5f'): According to the general procedure I, *N*-(2,2,4-trichlorobutylidene)*tert*-butylamine (**1f**) (0.5 mmol, 115 mg), phenylacetylene (**2b**) (1.0 mmol, 102 mg) and $In(OTf)_3$ (0.125 mmol, 70 mg) were reacted in DCM (4 mL) in a sealed vial at 50 °C for 18 h. Alkaline work up and column chromatography afforded trace amounts of **5f'** as a brownish oil. Yield: (22 mg, 21%) ;R_f = 0.21 (*n*-hexane/ethyl acetate 90/10). **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.16 (s, 9H, $C(CH_3)_3$), 2.49-2.66 (2H, m, CH_2CCl_2), 2.90- 3.00 (m, 1H, CH_aH_bN), 3.07-3.13 (m, 1H, CH_aH_bN), 4.77 (s, 1H, NC**H**OH). **IR** (ATR, cm^{-1}): ν = 3217 (**OH**). **HRMS** (ESI): *m/z* Calcd for $C_8H_{15}Cl_2NO+H^+$: 212.0603; Found 212.0616.

3,3-Dichloro-1-ethyl-2-(phenylethynyl)pyrrolidine (5a): dark brown oil; yield: (57 mg, 43%; Method II); R_f = 0.3 (*n*-hexane/ethyl acetate 85/15). **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.17 (3H, t, J = 7.1 Hz, NCH_2CH_3), 2.59 (dq, 1H, J_1 = 12.0 Hz, J_2 = 7.1 Hz, $NC(H)HCH_3$), 2.72-2.96 (m, 3H), 2.99-3.07 (m, 1H), 3.09-3.17 (m, 1H), 4.10 (s, 1H, $NCHCCl_2$), 7.29-7.34 (m, 3H), 7.48-7.52 (m, 2H). **^{13}C NMR** (62.90 MHz, $CDCl_3$): δ = 12.8 ($NCH_2\underline{C}H_3$), 45.9, 47.5, 49.3, 71.3 ($N\underline{C}HCCl_2$), 82.7 ($\underline{C}Cl_2$), 88.5 (C≡C), 89.1 (C≡C), 122.4, 128.3, 128.6, 132.0. IR (ATR, cm^{-1}): ν = 2237 (C≡C), 1490, 1443 (C=C aromate). **MS** (70 eV, *m/z* (%)): 271 ($[M+4]^+$, 2), 269 ($[M+2]^+$, 11), 267 (M^+, 30), 268 (10), 232 (9), 171 (84), 170 (83), 156 (100), 143 (26), 142 (64), 139 (25),

128 (11), 127 (9), 115 (41), 114 (29), 113 (15), 56 (26). **HRMS** (ESI): *m/z* Calcd for $C_{14}H_{15}Cl_2N+H^+$: 268.0654; Found 268.0653.

3,3-Dichloro-1-propyl-2-(phenylethynyl)pyrrolidine (5b): yellow oil; yield: (113 mg, 80%; Method I) or (65 mg, 46%; Method II); R_f = 0.3 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.95 (t, 3H, J = 8.0 Hz, $NCH_2CH_2C\mathbf{H_3}$), 1.57 (sextet, 2H, J = 8.0 Hz, $NCH_2C\mathbf{H_2}CH_3$), 2.52 (ddd, 1H, J_1 = 12.2 Hz, J_2 = 7.7 Hz, J_3 = 7.3 Hz), 2.72-2.89 (m, 4H), 3.03-3.12 (m, 1H), 4.11 (s, 1H, $NC\mathbf{H}CCl_2$), 7.30-7.32 (m, 3H), 7.47-7.50 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.8 ($NCH_2CH_2\underline{C}H_3$), 21.1 ($NCH_2\underline{C}H_2CH_3$), 45.8, 49.7, 55.3, 71.2 ($N\underline{C}HCCl_2$), 82.9 (C≡C), 88.4 (C≡C), 89.1 ($\underline{C}Cl_2$), 122.5, 128.2, 128.5, 131.9. **HRMS** (ESI): *m/z* Calcd for $C_{15}H_{17}Cl_2N+H^+$: 282.0811; Found 282.0826.

3,3-Dichloro-1-isopropyl-2-(phenylethynyl)pyrrolidine (5c): light brown oil; yield: (91 mg, 65%; Method I) or (45 mg 32%; Method II); R_f= 0.3 (cyclohexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.12 (d, 3H, J = 6.4 Hz, $CH(C\mathbf{H_3})CH_3$), 1.17 (d, 3H, J = 6.8 Hz, $CH(CH_3)C\mathbf{H_3}$), 2.69-2.85 (m, 2H), 2.93 (td, 1H, J_1 = 8.9 Hz, J_2 = 5.0 Hz), 3.02-3.06 (m, 1H), 3.09 (septet, 1H, J = 6.4 Hz), 4.35 (s, 1H, $NC\mathbf{H}CCl_2$), 7.30-7.31 (m, 3H), 7.46-7.48 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 18.9, 21.3, 45.4, 45.7, 50.9, 68.6 ($N\underline{C}HCCl_2$), 83.2 (C≡C), 88.5 (C≡C), 89.1 ($\underline{C}Cl_2$), 122.5, 128.2, 128.5, 131.9. **IR** (ATR, cm^{-1}): ν = 2238 (C≡C), 1574, 1544, 1490, 1443 (C=C aromate). **HRMS** (ESI): *m/z* Calcd for $C_{15}H_{17}Cl_2N+H^+$: 282.0811; Found 282.0827.

1-Allyl-3,3-dichloro-2-(phenylethynyl)pyrrolidine (5d): reddish oil; yield: (115 mg, 82%; Method I) or (56 mg, 40%; Method II); R_f = 0.2 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.73-2.84 (m, 3H), 3.03-3.12 (m, 1H), 3.22 (dddd, 1H, $NC\mathbf{H_c}\mathbf{H_d}CH=CH_2$, J_1 = 13.3 Hz, J_2 = 7.3 Hz, J_3 = 1.3 Hz), 3.59 (dddd, 1H, $NC\mathbf{H_c}\mathbf{H_d}CH=CH_2$, J_1 = 13.3 Hz, J_2 = 5.5 Hz, J_3 = 1.5 Hz), 4.13 (s, 1H, $NC\mathbf{H}CCl_2$), 5.18 (dddd, 1H, $NCH_2CH=CH_a\mathbf{H_b}$, J_1 = 10.0 Hz, J_2 = 2.8 Hz, J_3 = 1.3 Hz), 5.29 (dddd, 1H, $NCH_2CH=C\mathbf{H_a}H_b$, J_1 = 17.3 Hz, J_2 = 2.8 Hz, J_3 = 1.5 Hz), 5.93 (dddd, 1H, $NCH_2C\mathbf{H}=CH_2$, J_1 = 17.3 Hz, J_2 = 10.0 Hz, J_3 = 7.3 Hz, J_4 = 5.5 Hz), 7.30-7.32 (m, 3H), 7.48-7.50 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 45.9, 49.2, 55.9 ($N\underline{C}H_2CH=CH_2$), 70.7 ($N\underline{C}HCCl_2$), 82.5 (C≡C), 88.8 (C≡C), 88.9 ($\underline{C}Cl_2$), 118.5 ($NCH_2CH=\underline{C}H_2$), 122.3, 128.2, 128.6, 131.9, 133.9 ($NCH_2\underline{C}H=CH_2$). **IR** (ATR, cm^{-1}): ν = 2231 (C≡C), 1490, 1442, 1419 (C=C aromate), 1351, 1303, 1265 ($HC=CH_2$). **HRMS** (ESI): *m/z* Calcd for $C_{15}H_{15}Cl_2N+H^+$: 280.0654; Found 280.0672.

1-Butyl-3,3-dichloro-2-(phenylethynyl)pyrrolidine (5e): yellow oil; yield: (118 mg, 84%); R_f = 0.3 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.93 (t, 3H, J = 7.6 Hz, $NCH_2CH_2C\mathbf{H_3}$), 1.34-1.43 (m, 2H), 1.43-1.57 (m, 2H), 2.51 (ddd, 1H, J_1 = 12.3 Hz, J_2 = 9.1 Hz, J_3 = 6.1 Hz), 2.72-2.94 (m, 4H), 3.04-3.12 (m, 1H), 4.11 (s, 1H, $NC\mathbf{H}CCl_2$), 7.30-7.32 (m, 3H), 7.47-7.50 (m, 2H). **^{13}C NMR-APT** (100 MHz, $CDCl_3$): δ = 13.9, 20.5, 29.9, 45.8, 49.6, 53.1,71.3 ($N\underline{C}HCCl_2$), 83.0 (C≡C), 88.4 (C≡C), 89.1 ($\underline{C}Cl_2$), 122.5, 128.2, 128.5, 131.9. **HRMS** (ESI): *m/z* Calcd for $C_{16}H_{19}Cl_2N+H^+$: 296.0968; Found 296.0986.

3,3-Dichloro-1-propyl-2-(ortho-tolylethynyl)pyrrolidine (5f): yellow oil; yield: (101 mg, 68%); R_f= 0.4 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.96 (t, 3H, J = 7.4 Hz, $NCH_2CH_2C\mathbf{H_3}$), 1.57 (sextet, 2H, J = 7.5 Hz, $NCH_2C\mathbf{H_2}CH_3$), 2.47 (s, 3H, $C\mathbf{H_3}$), 2.55 (td, 1H, J_1 = 11.9 Hz, J_2 = 7.2 Hz), 2.74-2.90 (m, 4H), 3.02-3.10 (m, 1H), 4.18 (s, 1H, $NC\mathbf{H}CCl_2$), 7.14 (td,

1H, J_1 =7.0 Hz, J_2 = 2.0 Hz), 7.20-7.23 (m, 2H), 7.45 (d, 1H, J =7.5 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.8 ($NCH_2CH_2\underline{C}H_3$), 20.8, 21.1, 45.7, 49.6, 55.2, 71.2 ($N\underline{C}HCCl_2$), 86.7 (C≡C), 87.4 (C≡C), 89.1 ($\underline{C}Cl_2$), 122.3, 125.5, 128.5, 129.4, 132.3, 140.5. **HRMS** (ESI): *m/z* Calcd for $C_{16}H_{19}Cl_2N+H^+$: 296.0976; Found 296.0973.

3,3-Dichloro-1-propyl-2-(p-tolylethynyl)pyrrolidine (5g): yellow oil; yield: (105 mg, 71%); R_f = 0.4 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.95 (t, 3H, J = 7.3 Hz, $NCH_2CH_2C\mathbf{H_3}$), 1.57 (sextet, 2H, J = 7.5 Hz, $NCH_2C\mathbf{H_2}CH_3$), 2.35 (s, 3H, $C\mathbf{H_3}$), 2.51 (td, 1H, J_1 = 11.9 Hz, J_2 = 7.3 Hz), 2.73-2.90 (m, 4H), 3.10-3.03 (m, 1H), 4.10 (s, 1H, $NC\mathbf{H}CCl_2$), 7.37 (d, 2H, J = 8.0 Hz), 7.11 (d, 2H, J = 8.0 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.8 ($NCH_2CH_2\underline{C}H_3$), 21.1 ($NCH_2\underline{C}H_2CH_3$), 21.5, 45.8, 49.6, 55.3, 71.3 ($N\underline{C}HCCl_2$), 82.2 (C≡C), 88.6 (C≡C), 89.2 ($\underline{C}Cl_2$), 119.4, 129.0, 131.8, 138.7. **HRMS** (ESI): *m/z* Calcd for $C_{16}H_{19}Cl_2N+H^+$: 296.0968; Found 296.0979.

3,3-Dichloro-2-((4-ethylphenyl)ethynyl)-1-propylpyrrolidine (5h): dark yellow oil; yield: (119 mg, 72%); R_f= 0.5 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$):): δ = 0.95 (t, 3H, J = 7.4 Hz, $NCH_2CH_2C\mathbf{H_3}$), 1.22 (t, 3H, $CH_2C\mathbf{H_3}$, J = 7.6 Hz), 1.57 (sextet, 2H, J = 7.4 Hz, $NCH_2C\mathbf{H_2}CH_3$), 2.51 (td, 1H, J_1 = 12.1 Hz, J_2 = 7.3 Hz), 2.65 (q, 1H, J = 7.6 Hz, $C\mathbf{H_2}CH_3$), 2.74-2.88 (m, 4H), 3.03-3.10 (m, 1H), 4.11 (s, 1H, $NC\mathbf{H}CCl_2$), 7.14 (d, 2H, J = 8.3 Hz), 7.41 (d, 2H, J = 8.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.8 ($NCH_2CH_2\underline{C}H_3$), 15.4, 21.0, 28.8, 45.7, 49.7, 55.3, 71.3 ($N\underline{C}HCCl_2$), 82.1 (C≡C), 88.6 (C≡C), 89.1 ($\underline{C}Cl_2$), 119.6, 127.8, 131.9, 145.0. **HRMS** (ESI): *m/z* Calcd for $C_{17}H_{21}Cl_2N+H^+$: 310.1124; Found 310.1147.

3,3-Dichloro-2-((3-methoxyphenyl)ethynyl)-1-propylpyrrolidine (5i): yellow oil; yield: (110 mg, 71%); R_f= 0.3 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.95 (t, 3H, J = 7.4 Hz, $NCH_2CH_2C\mathbf{H_3}$), 1.58 (sextet, 2H, J =7.4 Hz, $NCH_2C\mathbf{H_2}CH_3$), 2.51 (td, 1H, J_1 = 12.0 Hz, J_2 = 7.2 Hz), 2.74-2.91 (m, 4H), 3.06-3.12 (m, 1H), 3.81 (s, 3H, $OC\mathbf{H_3}$), 4.11 (s, 1H, $NC\mathbf{H}CCl_2$), 6.89 (ddd, 1H, J_1 = 8.3 Hz, J_2 = 2.6 Hz, J_3 = 0.9 Hz), 7.02 (dd, 1H, J_1 = 2.4 Hz, J_2 = 1.4 Hz), 7.09 (dt, 1H, J_1 = 7.6 Hz, J_2 = 1.1 Hz), 7.23 (t, 1H, J = 8.0 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.8 ($NCH_2CH_2\underline{C}H_3$), 21.1 ($NCH_2\underline{C}H_2CH_3$), 45.8, 49.7, 55.3, 55.4, 71.3 ($N\underline{C}HCCl_2$), 82.8 (C≡C), 88.3 (C≡C), 89.1 ($\underline{C}Cl_2$), 115.2, 116.8, 123.4, 124.5, 129.3, 159.3. **HRMS** (ESI): *m/z* Calcd for $C_{16}H_{19}Cl_2NO+H^+$: 312.0917; Found 312.0916.

3,3-Dichloro-2-((4-chlorophenyl)ethynyl)-1-propylpyrrolidine (5j): yellow oil; yield: (96 mg, 61%); R_f= 0.3 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$):): δ = 0.95 (t, 3H, J = 7.3 Hz, $NCH_2CH_2C\mathbf{H_3}$), 1.57 (sextet, 2H, J = 7.4 Hz, $NCH_2C\mathbf{H_2}CH_3$), 2.50 (ddd, 1H, J_1 = 11.8 Hz, J_2 = 7.7 Hz, J_3 = 6.9 Hz), 2.73-2.89 (m, 4H), 3.05-3.14 (m, 1H), 4.09 (s, 1H, $NC\mathbf{H}CCl_2$), 7.29 (d, 2H, J = 8.6 Hz), 7.41 (d, 2H, J = 8.6 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.8 ($NCH_2CH_2\underline{C}H_3$), 21.0 ($NCH_2\underline{C}H_2CH_3$), 45.8, 49.7, 55.5, 71.4 ($N\underline{C}HCCl_2$), 88.9 ($\underline{C}Cl_2$), 120.9 (C_{quat}), 128.6 (C_{ortho}), 133.2 (C_{para}), 134.7 (C_{quat}). **HRMS** (ESI): *m/z* Calcd for $C_{15}H_{16}Cl_3N+H^+$: 316.0421; Found 316.0407.

3,3-Dichloro-2-((4-fluoro-3-methylphenyl)ethynyl)-1-propylpyrrolidine (5k): yellow oil; yield: (84 mg, 54%); R_f= 0.3 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.95 (t, 3H, J = 7.3 Hz, $NCH_2CH_2C\mathbf{H_3}$), 1.57 (sextet, 2H, J = 7.4 Hz, $NCH_2C\mathbf{H_2}CH_3$), 2.25 (d, 1H, J = 1.9 Hz, $C\mathbf{H_3}$), 2.46-2.57 (m, 1H), 2.73-2.87 (m, 4H), 3.04-3.11 (m, 1H), 4.09 (s, 1H, $NC\mathbf{H}CCl_2$), 6.94 (apparent t, 1H, J = 8.9 Hz), 7.27-7.34 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.8,

14.3 (d, J = 3.5 Hz), 45.8, 49.7, 55.4, 71.3 (N**C**HCCl$_2$), 82.2 (C≡C), 87.7 (C≡C), 89.1 (**C**Cl$_2$), 115.1 (d, J = 23.2 Hz), 118.1, 125.1 (d, J = 18.1 Hz), 131.2 (d, J = 8.4 Hz), 135.1 (d, J = 5.6 Hz), 161.3 (d, J = 248.6 Hz). **HRMS** (ESI): m/z Calcd for $C_{16}H_{18}NFCl_2$+H$^+$: 314.0873; Found 314.0888.

3,3-Dichloro-2-((4-bromophenyl)ethynyl)-1-propylpyrrolidine (5l): yellow oil; yield: (92 mg, 51%); R_f = 0.4 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 0.95 (t, 3H, J = 7.4 Hz, NCH$_2$CH$_2$C**H$_3$**), 1.56 (sextet, 2H, NCH$_2$C**H$_2$**CH$_3$, J = 7.4 Hz), 2.50 (td, 1H, J_1 = 12.1 Hz, J_2 = 7.3 Hz), 2.73-2.86 (m, 4H), 3.05-3.11 (m, 1H), 4.09 (s, 1H, N-C**H**CCl$_2$), 7.34 (d, 2H, J = 8.6 Hz), 7.45 (d, 2H, J = 8.6 Hz). **^{13}C NMR** (100 MHz, CDCl$_3$): δ = 11.8, 21.0, 29.7, 45.8, 49.8, 55.5, 71.4 (N**C**HCCl$_2$), 88.9 (**C**Cl$_2$), 112.9 (C≡C), 121.3 (C≡C), 131.6, 133.4. **HRMS** (ESI): m/z Calcd for $C_{15}H_{16}Cl_2BrN$+H$^+$: 359.9916; Found 359.9912.

3,3-Dichloro-2-(cyclohexylethynyl)-1-propylpyrrolidine (5m): yellow oil; (140 mg, 97%); R$_f$ = 0.4 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 0.93 (t, 3H, J = 7.3 Hz, NCH$_2$CH$_2$C**H$_3$**), 1.29-1.42 (m, 3H), 1.48-1.57 (m, 5H), 1.68-1.82 (m, 4H), 2.41 (ddd, 1H, J_1 = 11.8 Hz, J_2 = 7.3 Hz, J_3 = 6.6 Hz), 2.47-2.53 (m, 1H), 2.66-2.83 (m, 4H), 2.96-3.03 (m, 1H), 3.85 (d, 1H, J = 1.7 Hz, NC**H**CCl$_2$). **^{13}C NMR** (100 MHz, CDCl$_3$): δ = 11.8, 20.9, 24.5, 25.9, 28.9, 32.5, 45.7, 49.5, 55.2, 70.8, 73.5, 89.4, 93.3. **HRMS** (ESI): m/z Calcd for $C_{15}H_{23}Cl_2N$+H$^+$: 288.1280; Found 288.1299.

3,3-Dichloro-2-(cyclopentylethynyl)-1-propylpyrrolidine (5n): yellow oil; yield: (105 mg, 77%); R_f = 0.4 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 0.93 (t, 3H, J = 7.4 Hz, NCH$_2$CH$_2$C**H$_3$**), 1.52 (sextet, 2H, J = 7.4 Hz, NCH$_2$C**H$_2$**CH$_3$), 1.53-1.79 (m, 6H), 1.87-1.96 (m, 2H), 2.39 (ddd, 1H, J_1 = 11.7 Hz, J_2 = 7.3 Hz, J_3 = 6.5 Hz), 2.66-2.83 (m, 5H), 2.99-3.03 (m, 1H), 3.82 (d, 1H, J = 1.7 Hz, NC**H**CCl$_2$). **^{13}C NMR** (100 MHz, CDCl$_3$): δ = 11.8, 20.9, 24.8, 30.2, 33.8, 45.6, 49.5, 55.2, 70.9 (N**C**HCCl$_2$), 73.0, 89.4, 93.6. **HRMS** (ESI): m/z Calcd for $C_{14}H_{22}Cl_2N$+H$^+$: 274.1124; Found 274.1122.

3,3-Dichloro-2-(pent-1-ynyl)-1-propylpyrrolidine (5o): yellow oil; yield: (95 mg, 77%); R_f = 0.5 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 0.93 (t, 3H, J = 7.4 Hz, NCH$_2$CH$_2$C**H$_3$**), 1.01 (t, 3H, J = 7.4 Hz, NCH$_2$C**H$_2$**CH$_3$), 1.53 (sextet, 2H, J = 7.5 Hz), 1.61 (sextet, 2H, J = 7.2 Hz), 2.26 (td, 2H, J_1 = 6.9 Hz, J_2 = 1.8 Hz, C≡C-C**H$_2$**), 2.40 (td, 1H, J_1 = 12.0 Hz, J_2 = 7.3 Hz), 2.65-2.84 (m, 4H), 3.01-3.05 (m, 1H), 3.82 (brs, 1H, NC**H**CCl$_2$). **^{13}C NMR** (100 MHz, CDCl$_3$): δ = 11.8, 13.4, 20.8, 20.9, 22.0, 45.7, 49.5, 55.2, 70.9 (N**C**HCCl$_2$), 73.8, 89.0, 89.4. **HRMS** (ESI): m/z Calcd for $C_{12}H_{19}Cl_2N$+H$^+$: 248.0967; Found 248.0967.

3,3-Dichloro-2-(hex-1-ynyl)-1-propylpyrrolidine (5p): yellow oil; yield: (97 mg, 74%); R_f = 0.5 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 0.92 (t, 3H, J = 7.2 Hz), 0.93 (t, 3H, J = 7.3 Hz), 1.40- 1.57 (m, 6H), 2.28 (td, 2H, J_1 = 6.9 Hz, J_2 = 2.0 Hz, C≡C-C**H$_2$**), 2.38 (ddd, 1H, J_1 =11.7 Hz, J_2 = 8.2 Hz, J_3 = 6.6 Hz), 2.64-2.84 (m, 4H), 3.01-3.05 (m, 1H), 3.81 (t, 1H, NC**H**CCl$_2$, J = 2.0 Hz). **^{13}C NMR** (100 MHz, CDCl$_3$): δ = 11.8, 13.5, 18.5, 20.9, 21.8, 30.6, 45.6, 49.5, 55.3, 70.9 (N**C**HCCl$_2$), 73.5, 89.2, 89.3. **HRMS** (ESI): m/z Calcd for $C_{13}H_{22}Cl_2N$+H$^+$: 262.1124; Found 262.1140.

3,3-Dichloro-2-(3,3-dimethylbut-1-ynyl)-1-propylpyrrolidine (5q): yellow oil; yield: (92 mg, 70%); R_f = 0.4 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 0.93 (t, 3H, J = 7.4 Hz, N-CH$_2$CH$_2$C**H$_3$**), 1.26 (s, 9H, C(C**H$_3$**)$_3$), 1.54 (sextet, 2H, J = 7.4 Hz, NCH$_2$C**H$_2$**CH$_3$),

2.41 (ddd, 1H, J_1 = 11.7 Hz, J_2 = 8.1 Hz, J_3 = 6.6 Hz), 2.66-2.81 (m, 4H), 2.94-3.03 (m, 1H), 3.87 (s, 1H, NC**H**CCl_2). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.7 ($NCH_2CH_2\underline{C}H_3$), 20.8, 27.5, 30.8, 45.6, 49.6, 55.2, 70.6 (N**C**$HCCl_2$), 71.6, 89.2, 97.9. **HRMS** (ESI): *m*/*z* Calcd for $C_{13}H_{22}Cl_2N+H^+$: 262.1124; Found 262.1122.

General experimental procedure for the synthesis of 3-chloro-1*H*-pyrroles (6a-f): In a 50 mL round bottom flask 3,3-dichloropyrrolidine (**5b**, **5e**, **5g**, **5i**, **5k, 5p**) (0.25 mmol, 1 equiv) was dissolved in THF (5 mL) and the flask was closed with a drying tube. The resulting solution was allowed to stir for 10 min at 0 °C. Then, potassium *tert*-butoxide (0.75 mmol, 85 mg, 3 equiv) was added, which immediately resulted in a colored suspension. Subsequently the vessel was closed with a septum and equipped with a balloon of oxygen. After stirring for 12 hours at room temperature, the solvent was removed by means of a rotavapor. The residue was diluted with DCM (5 mL), washed with 0.5 N NaOH (4 mL) and H_2O (4 mL) to afford a pure mixture of (*E/Z*)-2-alkenyl-3-chloropyrroles (**6a-f**) and 3-chloro-2-(hex-1-ynyl)-1-propyl-1*H*-pyrrole (**7**).

(E)-3-Chloro-1-propyl-2-styryl-1H-pyrrole (6a)
Alkaline work up afforded pure mixture of (*E/Z*)-3-chloro-1-propyl-2-styryl-1*H*-pyrrole as a greenish oil. The overall yield of the mixture was 90% (55 mg). Compounds were separated using column chromatography to yield (*E*)-3-chloro-1-propyl-2-styryl-1*H*-pyrrole (**6a**) and (*Z*)-3-chloro-1-propyl-2-styryl-1*H*-pyrrole (**6b**). R_f = 0.6 (*n*-hexane/ethyl acetate 95/5) (overlapped spots for **6a**/**6b** were observed on TLC). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.93 (t, 3H, *J* = 7.2 Hz, $NCH_2CH_2C\mathbf{H_3}$), 1.78 (sextet, 2H, *J* = 7.2 Hz), 3.90 (t, 2H, *J* = 7.2 Hz, $NC\mathbf{H_2}CH_2CH_3$), 6.12 (d, 1H, *J* = 2.8 Hz), 6.58 (d, 1H, *J* = 2.8 Hz), 6.89 (d, 1H, J_{trans} = 16.4 Hz), 7.24 (d, 1H, J_{trans} = 16.4 Hz), 7.21-7.27 (m, 1H), 7.32-7.36 (m, 2H), 7.45-7.47 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.2, 24.4, 50.0, 108.9, 111.5, 115.5, 121.5, 126.0, 127.3, 128.5, 134.2, 138.0. **HRMS** (ESI): *m*/*z* Calcd for $C_{15}H_{16}ClN+H^+$: 246.1044; Found 246.1041.

(Z)-3-Chloro-1-propyl-2-styryl-1H-pyrrole (6b): **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.79 (t, 3H, *J* = 7.2 Hz, $NCH_2CH_2C\mathbf{H_3}$), 1.59 (sextet, 2H, *J* = 7.2 Hz), 3.53 (t, 2H, *J* = 7.6 Hz, $NC\mathbf{H_2}CH_2CH_3$), 6.09 (d, 1H, *J* = 2.8 Hz), 6.28 (d, 1H, J_{cis} = 12.0 Hz), 6.58 (d, 1H, *J* = 2.8 Hz), 6.68 (d, 1H, J_{cis} = 12.0 Hz), 7.10-7.13 (m, 1H), 7.17- 7.20 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.0, 24.2, 49.8, 108.1, 110.6, 116.9, 120.5, 125.5, 128.3, 131.2, 134.2, 137.0. **HRMS** (ESI): *m*/*z* Calcd for $C_{15}H_{16}ClN+H^+$: 246.1044; Found 246.1045.

(E/Z)-1-Butyl-3-chloro-2-styryl-1H-pyrrole (6c): yellow oil; yield (62 mg, 95%); R_f = 0.6 (*n*-hexane/ethyl acetate 95/5). The spots on TLC for *E*- and *Z*-isomers were too close, in order to perform a separation by means of flash chromatography. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.82 (t, 3H, *J* = 7.2 Hz, $NCH_2CH_2CH_2C\mathbf{H_3}$, *Z*), 0.93 (t, 3H, *J* = 7.6 Hz, $NCH_2CH_2CH_2C\mathbf{H_3}$, *E*), 1.33 (sextet, 2H, *J* = 7.2 Hz, $NCH_2CH_2C\mathbf{H_2}CH_3$, *Z*), 1.18 (sextet, 2H, *J* = 7.6 Hz, $NCH_2CH_2C\mathbf{H_2}CH_3$, *E*), 1.54 (quint, 2H, *J* = 7.2 Hz, $NCH_2C\mathbf{H_2}CH_2CH_3$, *Z*), 1.72 (quint, 2H, *J* = 7.6 Hz, $NCH_2C\mathbf{H_2}CH_2CH_3$, *E*), 3.55 (t, 2H, *J* = 7.2 Hz, $NC\mathbf{H_2}CH_2CH_2CH_3$, *Z*), 3.93 (t, 2H, *J* = 7.6 Hz, $NC\mathbf{H_2}CH_2CH_2CH_3$, *E*), 6.09 (d, 1H, *J* = 2.8 Hz, *Z*), 6.12 (d, 1H, *J* = 2.8 Hz, *E*), 6.28 (d, 1H, *J* = 12.0 Hz, *Z*), 6.56-6.57 (apparent t, 2H, *J* = 2.8 Hz), 6.68 (d, 1H, *J* = 12.0 Hz, *Z*), 6.89 (d, 1H, *J* = 16.4 Hz, *E*), 7.10-7.13 (m, 2H), 7.15-7.24 (d, 1H, *J* = 16.4 Hz & m, 4H), 7.32-7.36 (m, 2H), 7.44-7.47 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 13.5, 13.6, 19.7, 19.9, 33.0, 33.1, 47.9, 48.1, 108.1, 108.9, 110.5, 111.5, 115.5, 117.0, 120.4, 121.4, 125.49, 125.50, 126.0, 127.3, 127.6,

128.27, 128.32, 128.5, 128.7, 134.2, 137.1, 138.0. **HRMS** (ESI): *m*/*z* Calcd for $C_{16}H_{18}ClN+H^+$: 260.1201; Found 260.1211.

(E/Z)-3-Chloro-2-(4-methylstyryl)-1-propyl-1H-pyrrole (6d): brown oil; yield: (42 mg, 65%). R_f = 0.6 (*n*-hexane/ethyl acetate 95/5). The spots on TLC for *E*- and *Z*-isomers were too close, in order to perform a separation by means of flash chromatography. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.79 (t, 3H, *J* = 7.2 Hz, $NCH_2CH_2C\mathbf{H_3}$, *Z*-isomer), 0.93 (t, 3H, *J* = 7.6 Hz, $NCH_2CH_2C\mathbf{H_3}$, *E*-isomer), 1.60 (sextet, 2H, *J* = 7.2 Hz, $NCH_2C\mathbf{H_2}CH_3$, *Z*), 1.77 (sextet, 2H, *J* = 7.6 Hz, $NCH_2C\mathbf{H_2}CH_3$, *E*), 2.29 (s, 3H, $C\mathbf{H_3}$, *Z*), 2.35 (s, 3H, $C\mathbf{H_3}$, *E*), 3.54 (t, 2H, *J* = 7.2 Hz, $NC\mathbf{H_2}CH_2CH_3$, *Z*), 3.89 (t, 2H, *J* = 7.2 Hz, $NC\mathbf{H_2}CH_2CH_3$, *E*), 6.09 (d, 1H, *J* = 2.8 Hz, *Z*), 6.11 (d, 1H, *J* = 2.8 Hz, *E*), 6.22 (d, 1H, *J* = 12.0 Hz, *Z*), 6.56 (d, 1H, *J* = 2.8 Hz, *E*), 6.58 (d, 1H, *J* = 2.8 Hz, *Z*), 6.65 (d, 1H, *J* = 12.0 Hz, *Z*), 6.84 (d, 1H, *J* = 16.5 Hz, *E*), 7.01 (d, 2H, *J* = 9.2 Hz, *E*), 7.02 (d, 2H, *J* = 9.2 Hz, *E*), 7.15 (d, 2H, *J* = 8.0 Hz, *Z*), 7.21 (d, 2H, *J* = 16.8 Hz, *E*), 7.36 (d, 2H, *J* = 8.0 Hz, *Z*). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.0, 11.1, 21.1, 21.2, 24.32, 24.35, 49.9, 50.0, 108.0, 108.8, 110.3, 111.1, 114.6, 115.9, 120.3, 121.2, 125.6, 125.7, 125.9, 126.7, 128.3, 128.6, 128.9, 129.3, 131.1, 131.6, 134.1, 134.3, 135.2, 137.2, 137.4. **HRMS** (ESI): *m*/*z* Calcd for $C_{16}H_{18}ClN+H^+$: 260.1201; Found 260.1197.

(E/Z)-3-Chloro-2-(3-methoxystyryl)-1-propyl-1H-pyrrole (6e): yellow oil; yield: (61 mg, 88%); R_f = 0.6 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.78 (t, 3H, *J* = 7.2 Hz, $NCH_2CH_2C\mathbf{H_3}$, *Z*-isomer), 0.91 (t, 3H, *J* = 7.2 Hz, $NCH_2CH_2C\mathbf{H_3}$, *E*-isomer), 1.59 (sextet, 2H, *J* = 7.2 Hz, $NCH_2C\mathbf{H_2}CH_3$, *Z*), 1.76 (sextet, 2H, *J* = 7.2 Hz, $NCH_2C\mathbf{H_2}CH_3$, *E*), 3.53 (t, 2H, *J* = 7.2 Hz, $NC\mathbf{H_2}CH_2CH_3$, *Z*), 3.63 (s, 3H, $OC\mathbf{H_3}$, *Z*), 3.83 (s, 3H, $OC\mathbf{H_3}$, *E*), 3.89 (t, 2H, *J* = 7.2 Hz, $NC\mathbf{H_2}CH_2CH_3$, *E*), 6.09 (d, 1H, *J* = 2.8 Hz, *Z*), 6.12 (d, 1H, *J* = 2.8 Hz, *E*), 6.29 (d, 1H, *J* = 12.0 Hz, *Z*), 6.57 (apparent t (2 x d), 2 x 1 H, *J* = 2.8 Hz, *E* + *Z*), 6.67 (d, 1H, *J* = 12.0 Hz, *Z*), 6.67-6.69 (m, 1H, *E*), 6.73-6.75 (m, 2H, *E* + *Z*) 6.80 (ddd, 1H, *J* = 8.0, 2.5, 0.6 Hz, *E*), 6.88 (d, 1H, *J* = 16.4 Hz, *E*), 6.99 (t, 1H, *J* = 2.0 Hz, *E*), 7.05-7.07 (m, 1H, *E*), 7.11-7.15 (apparent t (dd), 1H, *J* = 8.0 Hz, *Z*), 7.21 (d, 1H, *J* = 16.4 Hz, *E*), 7.23-7.27 (m, 1H, *Z*). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.1, 11.2, 24.30, 24.4, 49.9, 50.0, 55.0, 55.3, 108.1, 108.9, 110.6, 111.61, 111.64, 112.5, 112.7, 114.2, 115.8, 117.2, 118.7, 120.5, 121.3, 121.6, 125.4, 128.3, 129.2, 129.5, 134.3, 138.2, 139.5, 159.4, 159.9. **HRMS** (ESI): *m*/*z* Calcd for $C_{16}H_{18}ClNO+H^+$: 276.1150; Found 276.1151.

E/Z-(3-Chloro-2-(4-fluoro-3-methylstyryl)-1-propyl-1H-pyrrole (6f): yellow oil; yield: (60 mg, 86%), R_f = 0.6 (*n*-hexane/ethyl acetate 95/5). The assignments in the ^{13}C NMR have been done by means of HMQC. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, 3H, *J* = 7.6 Hz, $NCH_2CH_2C\mathbf{H_3}$, *Z*-isomer), 0.93 (t, 3H, *J* = 7.2 Hz, $NCH_2CH_2C\mathbf{H_3}$, *E*-isomer), 1.60 (sextet, 2H, *J* = 7.3 Hz, $NCH_2C\mathbf{H_2}CH_3$, *Z*), 1.77 (sextet, 2H, *J* = 7.3 Hz, $NCH_2C\mathbf{H_2}CH_3$, *E*), 2.17 (d, 3H, $C\mathbf{H_3}$, *J* = 1.6 Hz, *Z*), 2.29 (d, 3H, $C\mathbf{H_3}$, *J* = 1.6 Hz, *E*), 3.54 (t, 2H, *J* = 7.6 Hz, $NC\mathbf{H_2}CH_2CH_3$, *Z*), 3.90 (t, 2H, *J* = 7.2 Hz, $NC\mathbf{H_2}CH_2CH_3$, *E*), 6.09 (d, 1H, *J* = 2.8 Hz, *Z*), 6.12 (d, 1H, *J* = 2.9 Hz, *E*), 6.23 (d, 1H, *J* = 11.9 Hz, *Z*), 6.57 (d, 1H, *J* = 2.9 Hz, *E*), 6.59 (d, 1H, *J* = 2.8 Hz, *Z*), 6.60 (d, 1H, *J* = 11.9 Hz, *Z*), 6.77 (d, 1H, *J* = 16.5 Hz, *E*), 6.80-7.00 (m, 3H, *E* and *Z*), 7.16 (d, 1H, *J* = 16.5 Hz, *E*), 7.22-7.28 (m, 1H, *E* and *Z*). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 11.0 ($\underline{\mathbf{C}}H_3CH_2$, *Z*), 11.1 ($\underline{\mathbf{C}}H_3CH_2$, *E*), 14.5 (d, *J* = 7.3 Hz, Ph$\underline{\mathbf{C}}H_3$, *Z*), 14.6 (d, *J* = 7.3 Hz, Ph$\underline{\mathbf{C}}H_3$, *E*), 24.30 ($CH_3\underline{\mathbf{C}}H_2$, *Z*), 24.35 ($CH_3\underline{\mathbf{C}}H_2$, *E*), 49.8 ($NCH_2$, *Z*), 49.9 ($NCH_2$, *E*), 108.1 ($CH_{pyrrole}$, *Z*), 108.8 ($CH_{pyrrole}$, *E*), 110.5 ($C_{quat}$), 111.3 ($C_{quat}$), 114.8 (d, *J* = 22.5 Hz, CH), 115.0 (d, *J* = 2.3 Hz, CH=$\underline{\mathbf{C}}$HAr, *E*), 115.3 (d, *J* = 22.7 Hz, CH), 116.3 (d, *J* = 1.9 Hz, CH=$\underline{\mathbf{C}}$HAr, *Z*), 120.5 ($CH_{pyrrole}$, *Z*), 121.4 ($CH_{pyrrole}$, *E*), 124.5 (d, *J* = 17.5 Hz, C_{quat}), 124.8 (d, *J* = 7.9 Hz, CH), 125.0 (d, *J* = 17.7 Hz, C_{quat}), 125.4 (d, *J* = 14.6 Hz,

C_{quat}), 127.18 (d, *J* = 8.0 Hz, CH), 127.7 (d, *J* = 0.9 Hz, **C**H=CHAr, *E*), 129.1 (d, *J* = 5.0 Hz, CH), 131.8 (d, *J* = 5.2 Hz, CH), 132.8 (d, *J* = 3.8 Hz, C_{quat}), 133.3 (**C**H=CHAr, *Z*), 133.8 (d, *J* = 3.7 Hz, C_{quat}), 160.7 (d, *J* = 246.7 Hz, C-F). 160.8 (d, *J* = 245.8 Hz, C-F). **HRMS** (ESI): *m*/*z* Calcd for $C_{16}H_{17}ClFN+H^+$: 278.1106; Found 278.1116.

3-Chloro-2-(hex-1-ynyl)-1-propyl-1H-pyrrole (7): scale**:** 0.34 mmol (90 mg); yellow oil; yield: (6 mg, 7%); R_f = 0.7 (*n*-hexane/ethyl acetate 90/10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3H, *J* = 7.4 , C**H$_3$**), 0.95 (t, 3H, *J* = 7.3 Hz, C**H$_3$**), 1.46-1.65 (m, 4H, $CH_2(CH_2)_2CH_3$), 1.77 (sextet, 2H, *J* = 7.3 Hz, $NCH_2CH_2CH_3$), 2.49 (t, 2H, *J* = 6.9 Hz, C**H$_2$**CH_2 CH_2CH_3), 3.85 (t, 2H, *J* = 7.1 Hz, NC**H$_2$**CH_2CH_3), 6.02 (d, 1H, *J* = 3.0 Hz); 6.49 (d, 1H, *J* = 3.0 Hz). No ^{13}C NMR and HRMS could be recorded due to fast degradation of the sample.

Experimental procedure for the borontrifluoride mediated synthesis of 3,3-dichloro-1-ethyl-2-styrylpyrrolidine (12a): To a stirred solution of the *N*-ethyl-(2,2,4-trichloro-1-butylidene)amines **1a** (0.5 mmol, 101 mg) in DCM/HFIP (9/1) (4 mL), potassium (2-phenyl)vinyltrifluoroborate (1 equiv, 0.5 mmol, 105 mg) was added in one portion, followed by $BF_3.OEt_2$ (1 equiv, 0.5 mmol, 71 mg). The reaction mixture was stirred for 18h at room temperature. Afterwards, the reaction mixture was poured into aqueous 0.5 N NaOH. After isolation of the organic layer, the aqueous phase was washed with DCM (4 × 4 mL). The organic fractions were dried using $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to obtain 77 mg (57%) of the pure 3,3-dichloropyrrolidine **12a** as a brown solid (mp: 62-64 °C).

3,3-Dichloro-1-ethyl-2-(2-phenylvinyl)pyrrolidine (12a): R_f = 0.26 (*n*-hexane/ethyl acetate 85/15). **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.10 (t, 3H, *J* = 7.2 Hz, NCH_2CH_3), 2.35 (dq, 1H, J_1 = 12.2 Hz, J_2 = 7.0 Hz), 2.51-2.59 (m, 1H), 2.69-2.80 (m, 1H), 2.80-2.94 (m, 2H), 3.30-3.38 (m, 1H), 3.42 (d, 1H, *J* = 8.1 Hz, NC**H**CCl_2), 6.20 (dd, 1H, J_1 = 15.9 Hz, J_2 = 8.1 Hz), 6.70 (d, 1H, *J* = 15.9 Hz), 7.20-7.40 (m, 3H), 7.40-7.50 (m, 2H). **^{13}C NMR** (62.90 MHz, $CDCl_3$): δ = 12.6, 46.5, 47.9, 49.4, 80.7, 91.6 (**C**Cl_2), 125.6, 126.8, 128.0, 128.6, 136.0, 136.4. **IR** (ATR, cm^{-1}): ν = 1497, 1479, 1451, 1441(C=C aromate), 1382, 1372, 1348, 1268 (CH=CH). **MS** (70 eV, *m/z* (%)): 271 ($[M+2]^+$, 2.8), 269 (M^+, 9.5), 234 (27), 174 (32), 173 (100), 158 (35), 141 (16), 117 (10), 115 (47), 96 (56), 91 (18), 56 (22). **HRMS** (ESI): *m*/*z* Calcd for $C_{14}H_{17}Cl_2N+H^+$: 270.0811; Found 270.0817.

Experimental procedure for the synthesis of 3-chloropyrroles 13a and 14a: In a 50 mL round bottom flask 3,3-dichloro-1-ethyl-2-(2-phenylvinyl)pyrrolidine (**12a**) (0.5 mmol, 135 mg) was dissolved in anhydrous THF (4 mL) and the flask was closed with a drying tube. The resulting solution was allowed to stir for 10 min at 0 °C. Then potassium *tert*-butoxide (3 equiv, 1.5 mmol) was added portionwise, that immediately resulted in a colored suspension. The reaction mixture was stirred for 3h at room temperature before it was quenched with water (4 mL) and extracted with Et_2O (4 mL-4 mL-3 mL). The organic fractions were dried over $MgSO_4$ and concentrated under reduced pressure. After flash chromatography on silica gel both pyrroles **13a** and **14a** were isolated in pure form.

3-Chloro-1-ethyl-2-(2-phenylvinyl)-1H-pyrrole (13a): Green oil; yield: (52 mg, 45%); R_f = 0.24 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.39 (t, 3H, *J* = 7.3 Hz, NCH_2CH_3), 3.98 (q, 2H, *J* = 7.3 Hz, NC**H$_2$**CH_3), 6.13 (d, 1H, *J* = 3.0 Hz), 6.73 (d, 1H, *J* = 3.0

Hz), 6.90 (d, 1H, *J* = 16.5 Hz), 7.21-7.37 (m, 4H), 7.45-7.49 (m, 2H). **^{13}C NMR** (62.90 MHz, $CDCl_3$): δ = 16.4 ($NCH_2\underline{C}H_3$), 43.0 ($N\underline{C}H_2CH_3$), 109.1, 111.5, 115.3, 120.5, 125.3, 126.0, 127.3, 128.5, 128.6, 137.9. **IR** (ATR, cm^{-1}): ν = 1630, 1597 (C=C aromates), 1482, 1448 (CH=CH). **MS** (70 eV, *m/z* (%)): 233 ($[M+2]^+$, 5), 232 ($[M^+$, 30), 196 (41), 180 (16), 169 (30), 167 (100), 139 (21), 63 (10). **HRMS** (ESI): *m/z* Calcd for $C_{14}H_{14}ClN+H^+$: 232.0888; Found 232.0897.

3-Chloro-1-ethyl-2-(2-phenylethyl)-1H-pyrrole (14a): scale: 1.85 mmol; dark green oil; yield: (151 mg, 35%); R_f = 0.31 (*n*-hexane/ethyl acetate 95/5). **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.25 (t, 3H, *J* = 7.3 Hz, $NCH_2C\mathbf{H_3}$), 2.83-2.87 (m, 4H), 3.62 (q, 2H, *J* = 7.3 Hz, $NC\mathbf{H_2}CH_3$), 6.06 (d, 1H, *J* = 3.0 Hz), 6.46 (d, 1H, *J* = 3.0 Hz), 7.12-7.31 (m, 5H). **^{13}C NMR** (62.90 MHz, $CDCl_3$): δ = 16.5 ($NCH_2\underline{C}H_3$), 26.1, 35.6, 41.8, 107.2, 109.0, 117.6, 126.1, 127.3, 128.39, 128.4, 141.2. **IR** (ATR, cm^{-1}): ν = 1603, 1492, 1452 (C=C aromates). **MS** (70 eV, *m/z* (%)): 235 ($[M+2]^+$, 2), 233 (M^+, 10), 145 (24), 144 (13), 142 (100), 114 (22), 91 (26), 65 (18), 51 (10). **HRMS** (ESI): *m/z* Calcd for $C_{14}H_{16}ClN+H^+$: 234.1044; Found 234.1049.

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Electronic Supplementary Information (ESI) available: ^{1}H and ^{13}C NMR spectra of starting imines (**1a-f**) and final compounds **5a-q**, **5c'**, **5f'**, **6a-f**, **7**, **12a, 13a** and **14a.**

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